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APPLICATION NUMBER: ***60/556,637***
FILING DATE: ***March 25, 2004***
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This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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032504

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Additional inventors are being named on the 1 separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

EMULSION-BASED CONTROL OF ELECTROSPUN FIBER MORPHOLOGY

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

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ENCLOSED APPLICATION PARTS (*check all that apply*)

[✓] Specification *Number of Pages* 14

[✓] Drawing(s) *Number of Sheets* 5

[✓] Application Data Sheet. See 37 CFR 1.76

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[✓] Other (specify) Fee Transmittal (in duplicate); Introductory Page; and Return Receipt Postcard

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[✓] Applicant claims small entity status. See 37 CFR 1.27.

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[✓] Yes, the name of the U.S. Government agency and the Government contract number are: R24-AI47739-03 (National Institute of Health)

Respectfully submitted,

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Date March 25, 2004

REGISTRATION NO. 52,328
(if appropriate)
Docket Number: T1118/20093

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Martha O. Hebert

Martha O. Hebert

PROVISIONAL APPLICATION COVER SHEET
Additional Page

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Docket Number T1118/20093

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☑ Applicant claims small entity status. See 37 CFR 1.27

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Complete if Known	
Application Number	Not Yet Known
Filing Date	March 25, 2004
First Named Inventor	Venkatram P. SHASTRI
Examiner Name	Not Yet Known
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1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
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2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		-20** =		X		=	
Independent Claims		- 3** =		X		=	
Multiple Dependent						=	

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1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

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FEE CALCULATION (continued)

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1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) ____________

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SUBMITTED BY (Complete *(if applicable)*)

Name *(Print/Type)*	Marina E. Volin	Registration No. (Attorney/Agent)	52,328	Telephone	215-567-2010
Signature	Marina E. Volin			Date	March 25, 2004

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Attorney Docket No. T1118/20093

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
APPLICATION FOR LETTERS PATENT

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INVENTION	:	EMULSION-BASED CONTROL OF ELECTROSPUN FIBER MORPHOLOGY
ATTORNEYS	:	Caesar, Rivise, Bernstein, Cohen & Pokotilow, Ltd. 12th Floor, Seven Penn Center 1635 Market Street Philadelphia, PA 19103-2212

TO ALL WHOM IT MAY CONCERN:

Be it known that I/We, the above-identified applicant(s), have made a certain new and useful invention in EMULSION-BASED CONTROL OF ELECTROSPUN FIBER MORPHOLOGY of which the following is a specification.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This research was supported in part by U.S. Government funds (National Institute of Health, grant number R24-AI47739-03), and the U.S. Government may therefore have certain rights in the invention.

EMULSION-BASED CONTROL OF ELECTROSPUN FIBER MORPHOLOGY

SPECIFICATION

BACKGROUND OF THE INVENTION

1. FIELD OF INVENTION

This invention relates to a process of making a fiber and more particularly to ways of modifying the fiber's morphology.

2. DESCRIPTION OF RELATED ART

Electrospinning (ES) is an atomization process of a conducting fluid which exploits the interactions between an electrostatic field and the conducting fluid. During electrospinning, fibers with micron or sub-micron sized diameters are extruded by means of an electrostatic potential from a polymer solution (see U.S. Patent No.1,975,504 to Formhals). When an external electrostatic field is applied to a conducting fluid (e.g., a semi-dilute polymer solution or a polymer melt), a suspended conical droplet is formed, whereby the surface tension of the droplet is in equilibrium with the electric field. Electrostatic atomization occurs when the electrostatic field is strong enough to overcome the surface tension of the liquid. The liquid droplet then becomes unstable and a tiny jet is ejected from the surface of the droplet. As it reaches a grounded target, the material can be collected as an interconnected web containing relatively fine, i.e. small diameter, fibers. The resulting films (or membranes) from these small diameter fibers have very large surface area to volume ratios and small pore sizes. This process typically yields non-woven mats or felts composed of round fibers that are extremely pliable. Due to their high-surface area and good mechanical characteristics, electrospun meshes have traditionally found applications in filtration and composite reinforcement. For the very same reasons, felts and meshes derived from biocompatible polymers such as poly(lactic acid) and its copolymer with glycolic acid and other polyesters are being explored as substrates (scaffolds) for association of cells in the engineering of tissue (see Kenawy et al., *Biomaterials*. 2003, *24(6)*, 907 describing making a fiber by electrospinning process from a single–phase system containing ethylene vinyl alcohol, 70% propanol and 30% water. Such pliable porous media are particularly suited for the engineering of skin, vascular and neural prosthesis.

A desired fiber property for tissue engineering (TE) applications is that it possesses a high aspect ratio to allow for cell attachment and spreading. The longest axis of a spread cell is typically around 5-10 microns. In general the ES process is not amenable to significant modifications. The only parameters that can be varied in the ES process are the electric field,

distance between the "Taylor Cone" and target, and polymer solution viscosity (Fridrikh et al., G.C. *Phys Rev Lett.* 2003, *90(14)*, 144502). Due to the complexity of the fiber forming process itself, very few attempts have been made to alter geometry of electrospun fibers. Recently, Reneker and co-workers have observed the formation of branched and ribbon-like fibers in some solvent systems and have attributed this to the collapse of a polymer skin due to buckling instability similar to that seen in garden hoses (see Koombhongse et al., *Polym. Sci.: Part B: Polym. Phys.* 2001, *39*, 2598 –2606). However, the formation of such fibers is not achievable in a predictable manner under generally known ES operating conditions.

U.S. Patent No. 4,323,525 is directed to a process for the production of tubular products by electrostatically spinning a liquid containing a fiber-forming material. The process involves introducing the liquid into an electric field through a nozzle, under conditions to produce fibers of the fiber-forming material, which tend to be drawn to a charged collector, and collecting the fibers on a charged tubular collector which rotates about its longitudinal axis, to form the fiberous tubular product. However, there is no suggestion or teaching of how to control the physical characteristics of the tubular product, other than by controlling the charge and rotation speed of the tubular collector. The spinning process of the '525 patent is used to fabricate tubular products having a homogenous fiber matrix across the wall thickness.

U.S. Patent No. 4,689,186 is directed to a process for the production of polyurethane tubular products by electrostatically spinning a fiber-forming liquid containing the polyurethane. The spinning process of the '186 patent is used to fabricate tubular products having a homogenous fiber matrix across the wall thickness.

Sanders et al. describe entrapment of water droplets in polyvinyl acetate fibers spun from a suspension containing the polymer in methylene chloride and protein (BSA) in a phospshate buffer. The composition is a cloudy suspension and not an emulsion. The ratio of organic solvent to water is 40:1 or about 2.4 vol%. There is no emulsifying agent such as poly(vinyl alcohol) used in the composition (see Macromolecules 2003, 36, 3803-3805).

Despite the foregoing development, it is desired to prove a method of making fibers with desirable morphology in a predicted and controllable manner.

All references cited herein are incorporated herein by reference in their entireties.

BRIEF SUMMARY OF THE INVENTION

The present invention provides a method of making a fiber comprising providing a first component comprising water, wherein the first component has a first evaporation rate, providing

a second component comprising a polymer, wherein the second component has a second evaporation rate, provided that the second evaporation rate is higher than the first evaporation rate, providing a solvent, combining the first component, the second component and the solvent to make an emulsion, applying a force to the emulsion, and extruding the emulsion to make the fiber, wherein the fiber has an outer surface, an internal cavity and a diameter of at most 10 microns.

In certain embodiments, the first component comprises at most 20 vol. % of the emulsion. In certain embodiments, the first component comprises from about 5 to about 20 vol. %. In certain embodiments, the first component comprises from about 2 to 5 vol. %.

In certain embodiments, the second component comprises at least 80% of the emulsion.

In certain embodiments, the first component comprises glycerol and poly(vinyl alcohol).

In certain embodiments, the polymer is a member selected from the group consisting of poly(styrene), poly(urethane), poly(lactic acid), poly(glycolic acid), poly(ester), poly(alpha-hydroxy acid), poly(ϵ-caprolactone), poly(dioxanone), poly(orthoester), poly(ether-ester), poly(lactone), poly(carbonate), poly(phosphazene), poly(phosphanate), poly(ether), poly(anhydride), mixtures thereof and copolymers thereof.

In certain embodiments, the solvent is a member selected from the group consisting of methylene chloride, chloroform, ether, hexane, pentane, petroleum ether, cresol, dichloroethane, ethyl acetate, methyl ethyl ketone, dioxane, propylene carbonate, and butyl acetate.

In certain embodiments, the method further comprises providing a third component, said third component is being a member selected from the group consisting of a biomolecule, a cell, a particle, a gel and a surfactant.

In certain embodiments, the biomolecule is a member selected from the group consisting of a bioactive polypeptide, a polynucleotide coding for the bioactive polypeptide, a cell regulatory small molecule, a peptide, a protein, an oligonucleotide, a nucleic acid, a poly(saccharide), an adenoviral vector, a gene transfection vector, a drug, and a drug delivering agent.

In certain embodiments, the cell is a member selected from the group consisting of chondroblast, chondrocyte, fibroblast, an endothelial cell, osteoblast, osteocyte, an epithelial cell, an epidermal cell, a mesenchymal cell, a hemopoietic cell, an embryoid body, a stem cell, and dorsal root ganglia.

In certain embodiments, the particle is a colloidal particle or a solid particle.

In certain embodiments, the colloidal particle has a diameter of from about 3nm to about 10 microns and said colloidal nanoparticle is a member selected from the group consisting of a polymer, an oxide, a nitride, a carbide, calcium silicate, calcium phosphate, calcium carbonate, a carbonaceous material, a metal, and a semiconductor.

In certain embodiments, the solid particle has a diameter of about 3nm to about 10 microns and said solid nanoparticle is a member selected from the group consisting of a polymer, an oxide, a nitride, a carbide, calcium silicate, calcium phosphate, calcium carbonate, a carbonaceous material, a metal, and a semiconductor.

In certain embodiments, the surfactant is a non-ionic surfactants such as, for example, PLURONIC, polyvinyl alcohol, poly(sorbate) (such as, for example, TWEEN-80 and SPAN-20), oleyl alcohol, glycerol ester, sorbitol, and carboxy methoxy cellulose or an ionic surfactant such as, for example, sodum dodecyl sulfonate, sodum dodecyl benzene sulfonate, oleic acid, albumin, ova-albumin, lecithin, natural lipids, and synthetic lipids.

In certain embodiments, the emulsion comprises water, poly(lactic acid), poly(vinyl alcohol) and optionally silicone oxide nanoparticle having a biomolecule attached to the nanopatricle's surface.

In certain embodiments, a source of the force is electric field. In certain embodiments, a source of the force is gas.

In certain embodiments, the fist component and the second component are provided at a ratio, wherein the ratio is adapted to change morphology of the fiber. In certain embodiments, the morphology is selected from the group consisting of flat fiber, round fiber, porous fiber and a combination thereof.

Also provided is a fiber manufactured by the method of the invention.

Further provided is a fiber made from the emulsion comprising water, poly(lactic acid), and optionally nanoparticle comprising silicone oxide and the biomolecule. In certain embodiments, the diameter of the fiber is from about 3 nm to 10 microns.

Also provided is an improvement to the method of making a fiber by electrospinning, the method comprising extruding a polymeric composition from a vessel through an orifice to form a fiber, the improvement wherein the composition comprises an emulsion comprising (1) a first component comprising water, said first component is provided in an amount of at most 20 vol. %, and (2) a second component comprising a polymer, said second component is provided in an amount of at least 80 vol. %, on a condition that the first component has a first evaporation rate

and the second component has a second evaporation rate and wherein the second evaporation rate is higher than the first evaporation rate.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

The invention will be described in conjunction with the following drawings in which like reference numerals designate like elements and wherein:

Fig. 1 shows poly(lactic acid) (PLA) fiber diameter and morphology as a function of volume fraction of aqueous phase in the water/oil (W/O) emulsion.

Fig. 2 shows PLA fibers obtained by spinning from a single-phase system composed of chloroform and 1-methyl-2-pyrrolidinone (NMP).

Fig. 3 shows PLA fibers obtained by spinning from a W/O emulsion composed of 2.5 v/v % aqueous phase; the porous nature of the fibers is shown in the inset on the bottom left.

Fig. 4 shows PLA fibers obtained by spinning from a W/O emulsion composed of 14 v/v % aqueous phase.

Fig. 5 shows PLA fibers obtained by spinning from a W/O emulsion composed of 885 μl PLA, 27 μl NMP, 0 μl PVA(10%) and 100 μl colloid (sample E4).

Fig. 6 shows PLA fibers obtained by spinning from a W/O emulsion composed of 835 μl PLA, 25 μl NMP, 50 μl PVA, and 100 μl Colloid/Water (sample E2).

Fig. 7 shows PLA fibers obtained by spinning from a W/O emulsion composed of 835 μl PLA, 25 μl NMP, 50 μl PVA, and 100 μl Colloid/Water (sample E2).

Fig. 8 shows PLA fibers obtained by spinning from a W/O emulsion composed of 980 μl PLA, 80 μl NMP, 2.5 μl PVA and 2.5 μl Colloid/Water (sample WC4).

Fig. 9 shows PLA fibers obtained by spinning from a W/O emulsion composed of 1 g of Alginate Beads suspended in about 2 ml E4 sample and 125 μl Colloid/Water (sample AB8).

Fig. 10 shows PLA fibers obtained by spinning from a W/O emulsion composed of 1 g of Alginate Beads suspended in about 2 ml E4 sample and 125 μl Colloid/Water (sample AB8).

DETAILED DESCRIPTION OF THE INVENTION

Inventors have discovered that that fiber morphology may be varied by spinning from a multi-phasic solution. Specifically, by using two solvent systems of varying evaporation rates and miscibility, a preferential evaporation of the more volatile solvent will result in the formation of skins similar to sausage casing, where the less volatile liquid phase is entrapped and surrounded by a solidified polymer skin. This evolution should facilitate the further development of different fiber morphology, including flattened ones and porous ones. Being

able to control morphology of the fiber is useful in various application such as for example tissue engineering, drug delivery, as well as other non-medical application such as for example electronics. Inventors have discovered that control over morphology can be achieved by using a water/oil emulsion. Surprisingly, to date, much of research in ES has focused on spinning from single-phase solutions. This invention discloses the effect of a water/oil emulsion on the morphology of poly(L-lactic acid) (PLA) fibers obtained by ES.

Apparatuses useful in this invention are known in the art such as, for example, the electrospinner described by Fridrikh et al., supra. Another type of apparatus employs a compressed gas as described by U. S. Patent No. 6,520,425 by Reneker.

Experimental

Materials: Poly(L-lactic acid) (MW=300,000) (PLA) was purchased from Polysciences, Inc. (Warrington, PA). Poly(vinyl alcohol) (MW=10,000, 85% hydrolyzed) (PVA) and 1-methyl-2-pyrrolidinone (99.5%) (NMP) were purchased from Aldrich Chemical Co (Milwaukee, WI). Chloroform (HPLC grade, 99.8%) was purchased from Fisher Scientific (Pittsburgh, PA). Poly(acrylic acid) coated Silica colloids 500 nm in diameter were produced by a sol-gel process. All chemicals were used as received without further purification unless otherwise noted.

Preparation of Polymer Solutions. Water-in-oil (W/O) emulsion of PLA was prepared by emulsifying a 2% stock of PLA in chloroform with 5% PVA solution in water and a fixed volume of NMP (Table 1). NMP was added to the mixture to serve as a phase compatibilizer (NMP is soluble in both water and chloroform) and to retard the evaporation of chloroform (oil phase). Formulations containing varying amounts of aqueous phase and PVA were studied and are shown in Table 1. To aid in the analysis of the evolution of fiber morphology and get an insight into the mechanism of fiber formation silica colloids (< 1% v/v) were added to some of the formulations. All components were metered using Eppendorf pipette, mixed by vortexing and sonicated for 45 seconds (20 KHz, Vibra Cell, Sonic Systems) to ensure full emulsification.

Electrospinning of PLA fibers. The polymer solution (typical volume 1 ml) was loaded into a 3 ml syringe fitted with a 16-gauge blunt tip needle. The syringe was mounted on a ring stand at a 45° angle below horizontal. The needle was connected to a high voltage power supply (Gamma High Voltage Research, Ormond Beach, FL). The counter electrode was connected to an aluminum foil (collecting target) placed at a distance of 15 cm away from the tip of the needle. The bias between each plate was then slowly increased until the eruption of the "Taylor

Cone" and was then set at 25 kV. Fibers were collected on the aluminum foil until the solution was fully dispensed.

Fiber Characterization. Electrospun fibers were imaged using a JEOL 6300FV field emission scanning electron microscope at an acceleration voltage of 10 KeV. Samples were mounted onto aluminum stubs using conductive carbon tape and then sputter coated with Pd-C to minimize charging. TIFF files of the images were then imported into Scion Image (NIH, Bethesda, MD) for analysis.

Table 1. Polymer solution composition (v/v %)

Formulation	% PVA	% Water
C1	0.0	0.0
WC2	2.2	2.5
W1	6.1	4.9
C2	8.9	5.2
WC1	4.4	4.9
E3	8.7	7.4
E2	9.1	14.9
V3	1.0	5.7
V2	1.9	6.2
E1	8.8	9.9
V4	16.2	14.1

Table 2 Description of composition of samples

Sample	Composition	Sample	Composition
C1	990 μl PLA 30 μl NMP	V3	885 μl PLA 27 μl NMP 50 μl PVA (0.5%) 50 μl Colloid/Water
C2	885 μl PLA 27 μl NMP 50 μl PVA 50 μl Water	AB8	1 g of Alginate Beads suspended in ~ 2 ml E4 solution 125 μl Colloid/Water
C3	885 μl Chloroform 27 μl NMP 50 μl PLA 50 μl Water	WC1	935 μl PLA 29 μl NMP 25 μl PVA 25 μl Colloid/Water
E1	885 μl PLA 27 μl NMP 50 μl PVA 50 μl Colloid/Water	WC2	960 μl PLA 29 μl NMP 12.5 μl PVA 12.5 Colloid/Water

Sample	Composition	Sample	Composition
E2	835 μl PLA 25 μl NMP 50 μl PVA 100 μl Colloid/Water	WC3	975 μl PLA 30 μl NMP 5 μl PVA 5μl Colloid/Water
E3	905 μl PLA 27 μl NMP 50 μl PVA 25 μl Colloid/Water	WC4	980 μl PLA 80 μl NMP 2.5 μl PVA 2.5 μl Colloid/Water
E4	885 μl PLA 27 μl NMP 10 μl PVA(10%) 100 μl Colloid	WC5	485 μl PLA 15 μl NMP 250 μl PVA 250 μl Colloid/Water
EL4	885 μl PLA 27 μl NMP 10 μl PVA(10%) 100 μl Ludox Colloid	WC6	730 μl PLA 23 μl NMP 125 μl PVA
V1	885 μl PLA 27 μl NMP 50 μl PVA (2.5%) 50 μl Colloid/Water	WC7	830 μl PLA 26 μl NMP 75 μl PVA 75 μl Colloid/Water
V2	885 μl PLA 27 μl NMP 50 μl PVA (1%) 50 μl Colloid/Water	WC8	785 μl PLA 24 μl NMP 100 μl PVA 100 μl Colloid/Water

Note: all PLA 2% in chloroform and all PVA 5% in water unless noted otherwise.
Electrospinning Parameters: 25kV, 16G Blunt Needle Tip, 15 cm tip to target distance, 45° Syringe Angle

Results and Discussion

In this experiments, W/O emulsions of PLA dissolved in a chloroform/NMP mixture and water, stabilized by PVA, were used as a model two-phase system to study its effect on fiber morphology in the ES process. The choice of this system was driven by two considerations, namely, easy adaptability to biomedical applications and biocompatibility of the non-volatile components. Solutions containing up to 15% aqueous phase were successfully electrospun without any disruption of the fiber morphology. However solutions that contained greater than 20% by volume of aqueous phase tended to spray as droplets suggesting the onset of instability of the "Taylor Cone". We observed that by varying the volume fraction of the aqueous phase the morphology and diameter of ES PLA fibers could be significantly impacted. In general, increasing the volume fraction of the aqueous phase yielded fibers with smaller diameters (Figure 1). One contributing factor could be the lower volume fraction of polymer at higher

aqueous phase concentrations. Rheological effects are most likely the dominant component of the fiber-thinning process. However, we observed no correlation between PVA concentration and fiber diameter. An interesting outcome of this process is that an order of magnitude change in fiber diameter can be achieved with the introduction of a small volume fraction of aqueous phase. The fiber diameter data can be fitted to an exponential decay process, which is consistent with a trend one may observe with respect to the stability of emulsions. The typical fiber morphology obtained in the ES process is that of a circular rod (Figure 2). However, in our system by selecting appropriate emulsion compositions fiber morphology may be varied from round spaghetti-like, to porous (Figure 3), to flat ribbon-like fibers (Figure 4) without varying the conditions of the ES process, namely the bias. SEM analyses of the fibers reveal that the transition from round to porous fibers occurs in the range of 2-5% volume fraction of aqueous phase in the emulsion. Above 5% volume fraction of aqueous phase, fibers with a flat-ribbon morphology are obtained. This transition may be explained as follows. At lower aqueous phase volume fractions, the emulsion droplets are relatively stable and there is no further segregation for the entire duration of ES. As the emulsion solution is propelled towards the target the polymer fraction, which constitutes the vast majority undergoes solidification due to the evaporation of the volatile organic phase (chloroform) and the resulting fiber then gets stretched as it approaches the target, while the aqueous phase remains entrapped within the rapidly solidifying polymer (oil) phase. The aqueous droplets become regions of instability toward the later stage of solidification as it constitutes a larger portion of the liquid phase, and a surface tension driven phase segregation process can result yielding porous fibers upon the evaporation of the aqueous component. At still higher volume fractions of aqueous phase, the stability of the emulsion is rather poor even at the early stage of ES and solidification and this leads to a rapid phase segregation and the encapsulation of larger water droplets within the solidifying polymer phase. As the polymer skin evolves the aqueous phase coalesce to yield a structure similar to water filled balloon or garden hose. The polymer skin eventually collapses, probably after partial evaporation of the entrapped aqueous phase, because of buckling instability in bending a thin wall tube. This yields fibers with flat ribbon-like morphologies. The proposed mechanism has also been verified in part through indirect observations in systems containing silica colloids.

In addition to utilizing emulsions to vary fiber morphology, a two-phase system can be used to incorporate other bioactive molecules or particles, such as enzymes or drugs, into the fibers. We have examined this possibility by encapsulating silica nanoparticles (SNP) within

polymer fibers. The presence of SNP within the fibers was verified using SEM and BET measurements, which revealed the presence of a phase with a very high surface area (> 50 m2/gm). Patterning the surfaces of fibers has practical applications in tissue engineering where presentation of chemical and physical cues on degradable scaffolds allows a more precise control over cell-scaffold interactions. One may also use the system described herein to incorporate conductive species such as carbon nanotubes and magnetic species to impart various bulk characteristics.

Conclusions

Most attempts at controlling fiber morphology have utilized solution viscosity and secondary electric fields. Emulsion-based control is a more readily modifiable parameter. We have been able to produce porous to ribbon-like fiber morphology as well as encapsulate solid particles using this system. The addition of aqueous phase produces fibers with smaller diameters, compared to single-phase PLA solution of identical polymer concentration. Electrospinning from biphasic solutions present a number of potential benefits. For example, it would enable the encapsulation of bioactive molecules in large concentrations with potential applications in the development of anti-bio-warfare systems, drug delivery, wound healing and tissue engineering. Our lab is currently investigating the effects of different surfactants (ionic and non-ionic) and solid particulate phase in the evolution of fiber morphology in this system.

While the invention has been described in detail and with reference to specific examples thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of making a fiber, the method comprising:

providing a first component comprising water, wherein the first component has a first evaporation rate;

providing a second component comprising a polymer, wherein the second component has a second evaporation rate, provided that the second evaporation rate is higher than the first evaporation rate;

providing a solvent;

combining the first component, the second component and the solvent to make an emulsion;

applying a force to the emulsion; and

extruding the emulsion to make the fiber, wherein the fiber has an outer surface, an internal cavity and a diameter of at most 10 microns.

2. The method of claim 1, wherein the first component comprises at most 20 vol. % of the emulsion.

3. The method of claim 1, wherein the first component comprises from about 5 to about 20 vol. %.

4. The method of claim 1, wherein the first component comprises from about 2 to 5 vol. %.

5. The method of claim 1, wherein the second component comprises at least 80% of the emulsion.

6. The method of claim 1, wherein the first component comprises glycerol and poly(vinyl alcohol).

7. The method of claim 1, wherein the polymer is a member selected from the group consisting of poly(styrene), poly(urethane), poly(lactic acid), poly(glycolic acid), poly(ester), poly(alpha-hydroxy acid), poly(ϵ-caprolactone), poly(dioxanone), poly(orthoester), poly(ether-ester), poly(lactone), poly(carbonate), poly(phosphazene), poly(phosphanate), poly(ether), poly(anhydride), mixtures thereof and copolymers thereof.

8. The method of claim 1, wherein the solvent is a member selected from the group consisting of methylene chloride, chloroform, ether, hexane, pentane,

petroleum ether, cresol, dichloroethane, ethyl acetate, methyl ethyl ketone, dioxane, propylene carbonate, and butyl acetate.

9. The method of claim 1, further providing a third component, said third component is being a member selected from the group consisting of a biomolecule, a cell, a particle, a gel and a surfactant.

10. The method of claim 9, wherein the biomolecule is a member selected from the group consisting of a bioactive polypeptide, a polynucleotide coding for the bioactive polypeptide, a cell regulatory small molecule, a peptide, a protein, an oligonucleotide, a nucleic acid, a poly(saccharide), an adenoviral vector, a gene transfection vector, a drug, and a drug delivering agent.

11. The method of claim 9, wherein the cell is a member selected from the group consisting of chondroblast, chondrocyte, fibroblast, an endothelial cell, osteoblast, osteocyte, an epithelial cell, an epidermal cell, a mesenchymal cell, a hemopoietic cell, an embryoid body, a stem cell, and dorsal root ganglia.

12. The method of claim 9, wherein the particle is a colloidal particle or a solid particle.

13. The method of claim 12, wherein the colloidal particle has a diameter of from about 3nm to about 10 microns and said colloidal nanoparticle is a member selected from the group consisting of a polymer, an oxide, a nitride, a carbide, calcium silicate, calcium phosphate, calcium carbonate, a carbonaceous material, a metal, and a semiconductor.

14. The method of claim 12, wherein the solid particle has a diameter of about 3nm to about 10 microns and said solid nanoparticle is a member selected from the group consisting of a polymer, an oxide, a nitride, a carbide, calcium silicate, calcium phosphate, calcium carbonate, a carbonaceous material, a metal, and a semiconductor.

15. The method of claim 9, wherein the surfactant is a member selected from the group consisting of PLURONIC, polyvinyl alcohol, poly(sorbate), oleyl alcohol, glycerol ester, sorbitol, carboxy methoxy cellulose, sodum dodecyl sulfonate, sodum dodecyl benzene sulfonate, oleic acid, albumin, ova-albumin, lecithin, natural lipids, and synthetic lipids.

16. The method of claim 1, wherein the emulsion comprises water, poly(lactic acid), poly(vinyl alcohol) and optionally silicone oxide nanoparticle comprising a biomolecule.

17. The method of claim 1, wherein a source of the force is electric field.

18. The method of claim 1, wherein a source of the force is gas.

19. The method of claim 1, wherein the fist component and the second component are provided at a ratio, wherein the ratio is adapted to change morphology of the fiber.

20. The method of claim 19, wherein the morphology is a member selected from the group consisting of flat fiber, round fiber, porous fiber and a combination thereof.

21. A fiber manufactured by the method of claim 1.

22. The fiber of claim 21, wherein the emulsion comprises water, poly(lactic acid), and optionally a nanoparticle comprising silicone oxide and the biomolecule.

23. The fiber of claim 21, wherein the diameter is from about 3 nm to 10 microns.

24. In a method of making a fiber by electrospinning comprising extruding a polymeric composition from a vessel through an orifice to form a fiber, the improvement wherein the composition comprises an emulsion comprising (1) a first component comprising water, the first component is provided in an amount of at most 20 vol. %, and (2) a second component comprising a polymer, the second component is provided in an amount of at least 80 vol. %, on a condition that the first component has a first evaporation rate and the second component has a second evaporation rate and wherein the second evaporation rate is higher than the first evaporation rate.

ABSTRACT OF THE DISCLOSURE

The invention provides a fiber having different morphology and a method of making such fiber in a predictable manner. The method includes providing a first component including water, wherein the first component has a first evaporation rate, providing a second component including a polymer, wherein the second component has a second evaporation rate, provided that the second evaporation rate is higher than the first evaporation rate, providing a solvent, combining the first component, the second component and the solvent to make an emulsion, applying a force to the emulsion, and extruding the emulsion to make the fiber, wherein the fiber has an outer surface, an internal cavity and a diameter of at most 10 microns.

Fig. 1

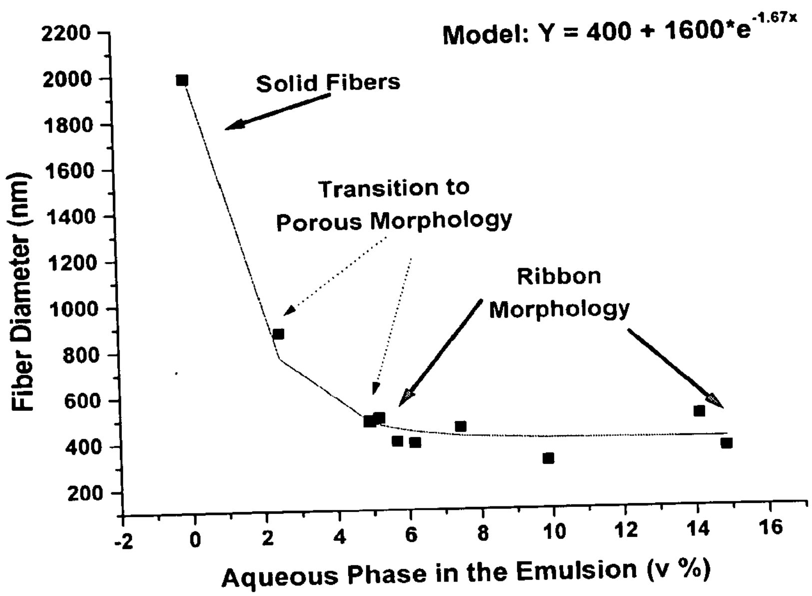

Model: Y = 400 + 1600*e^-1.67x
Solid Fibers
Transition to Porous Morphology
Ribbon Morphology
Fiber Diameter (nm)
Aqueous Phase in the Emulsion (v %)
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
-2
0
2
4
6
8
10
12
14
16

Fig. 2

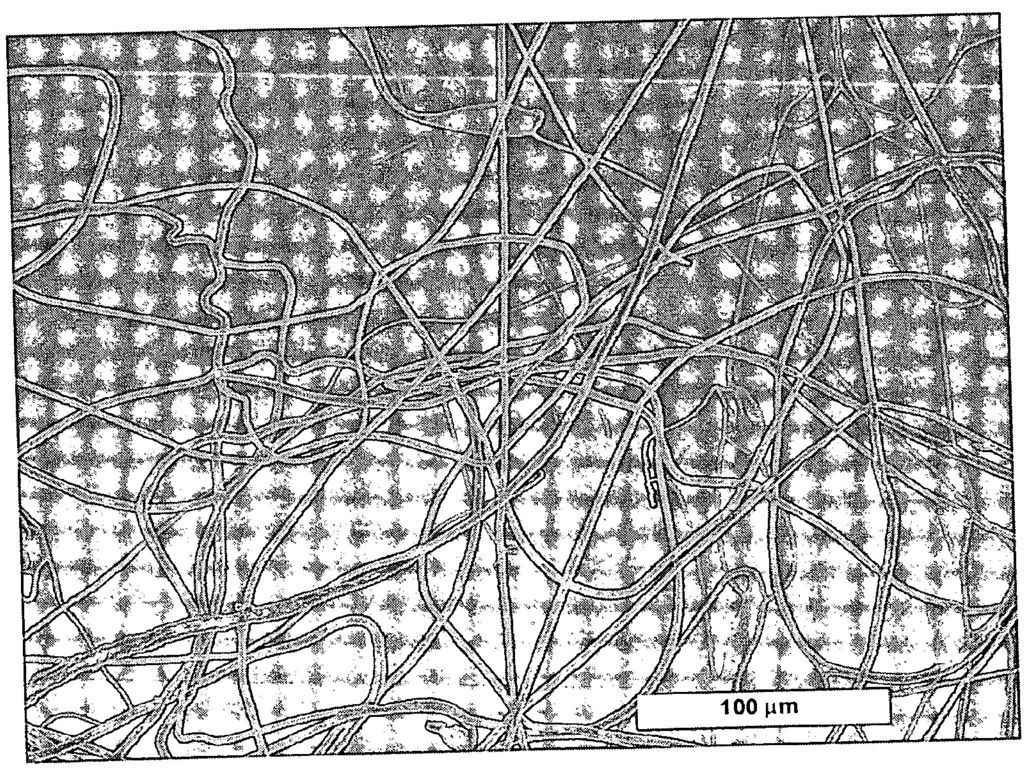

100 µm

Fig. 3

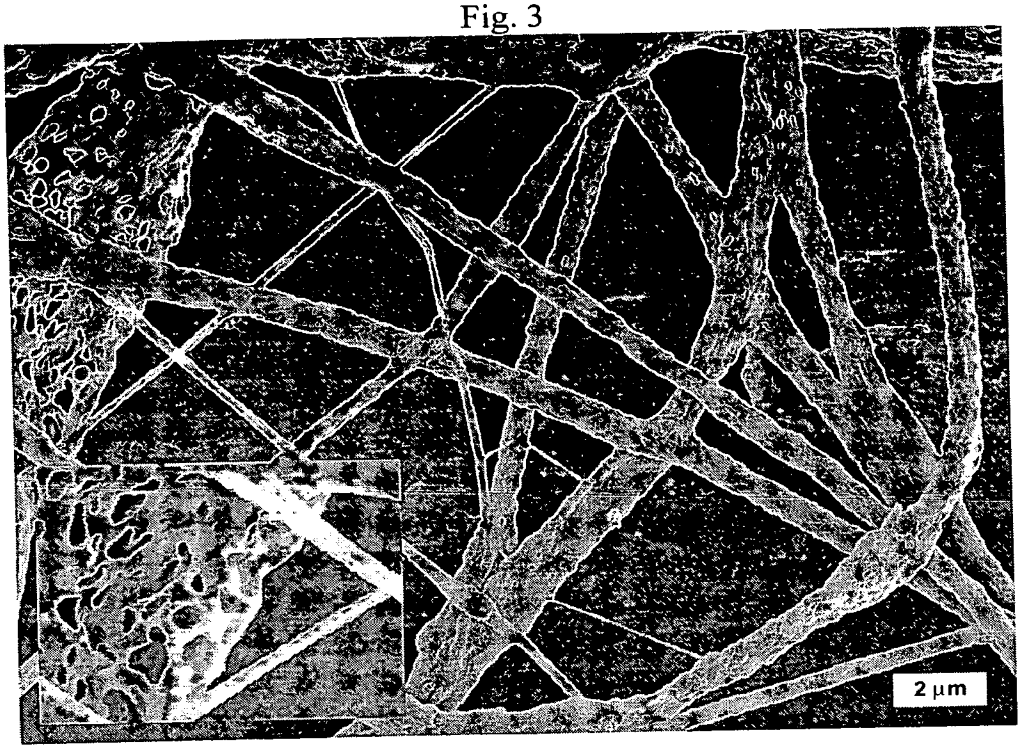


Fig. 4

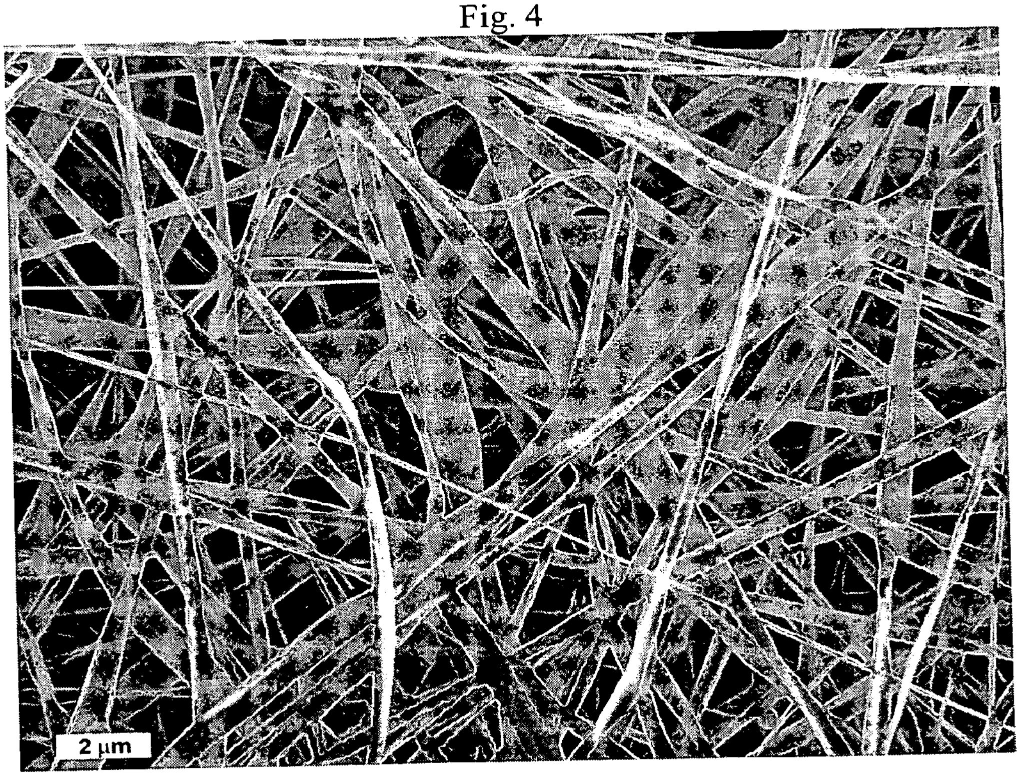
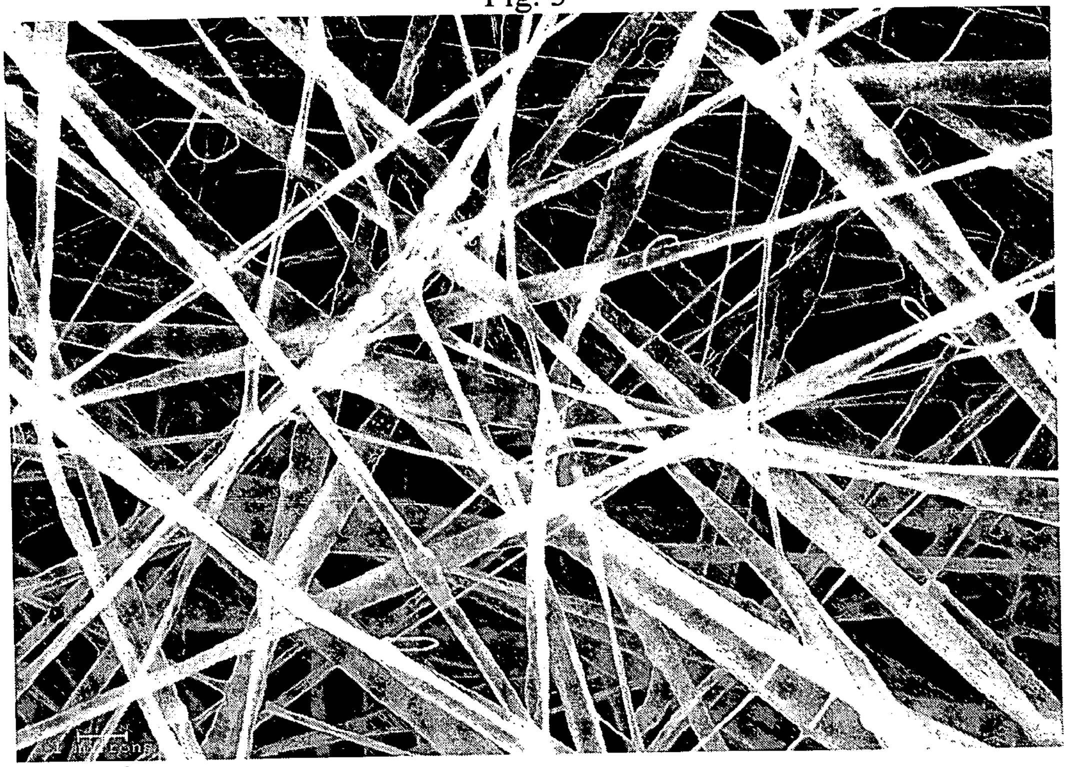


Fig. 5



1 micron

Fig. 6

1 micron

Fig. 7

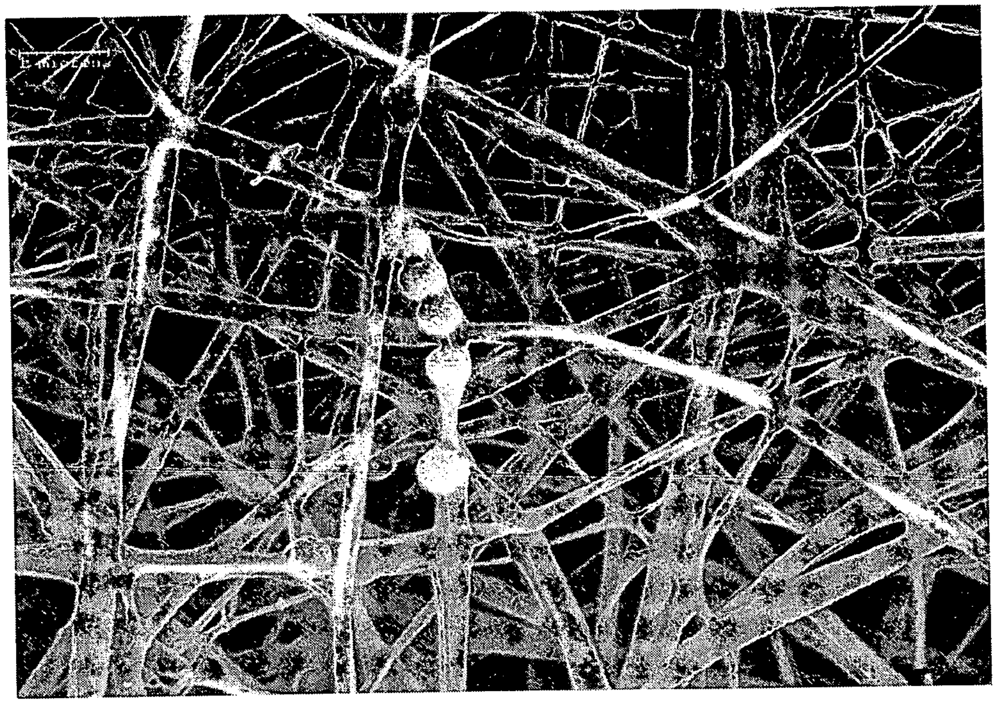


Fig. 8

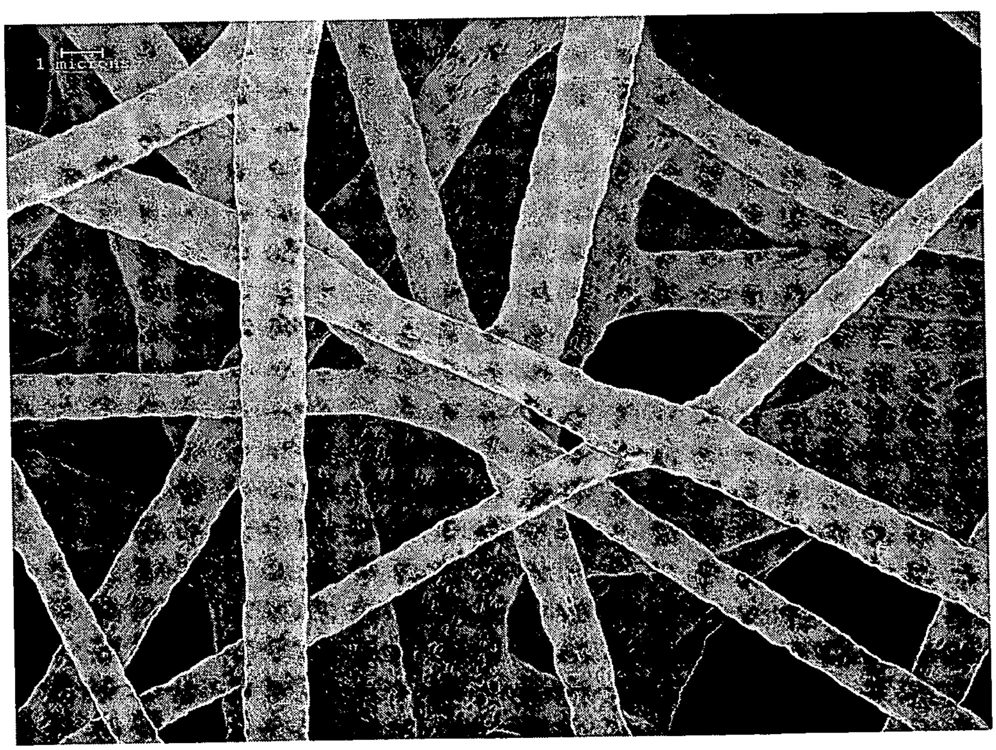


Fig. 9

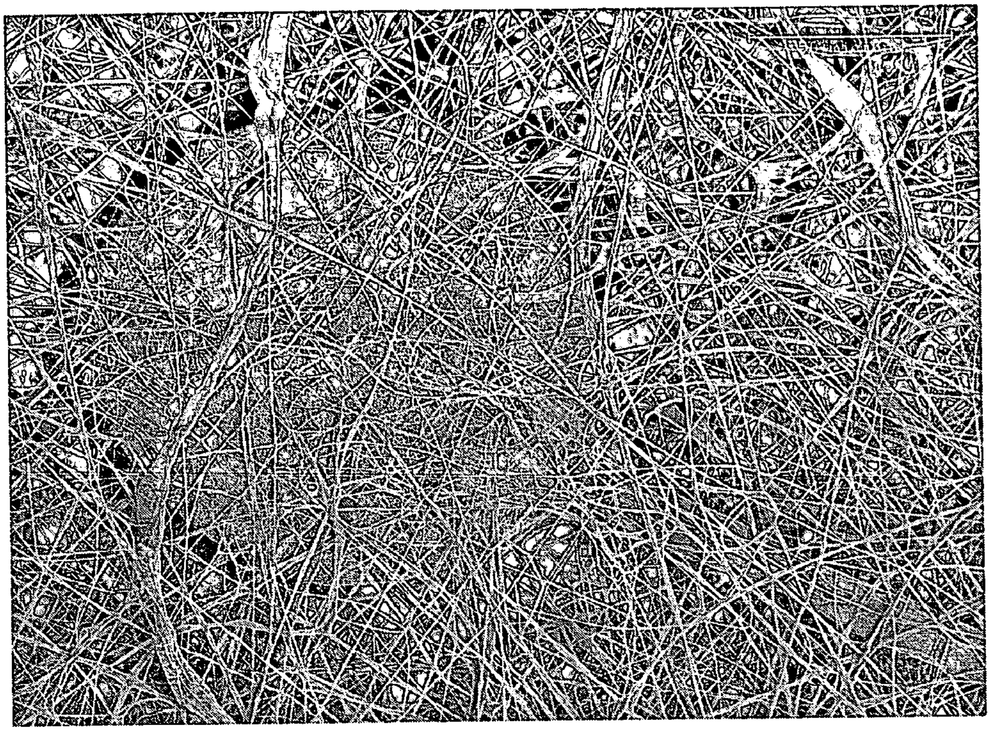
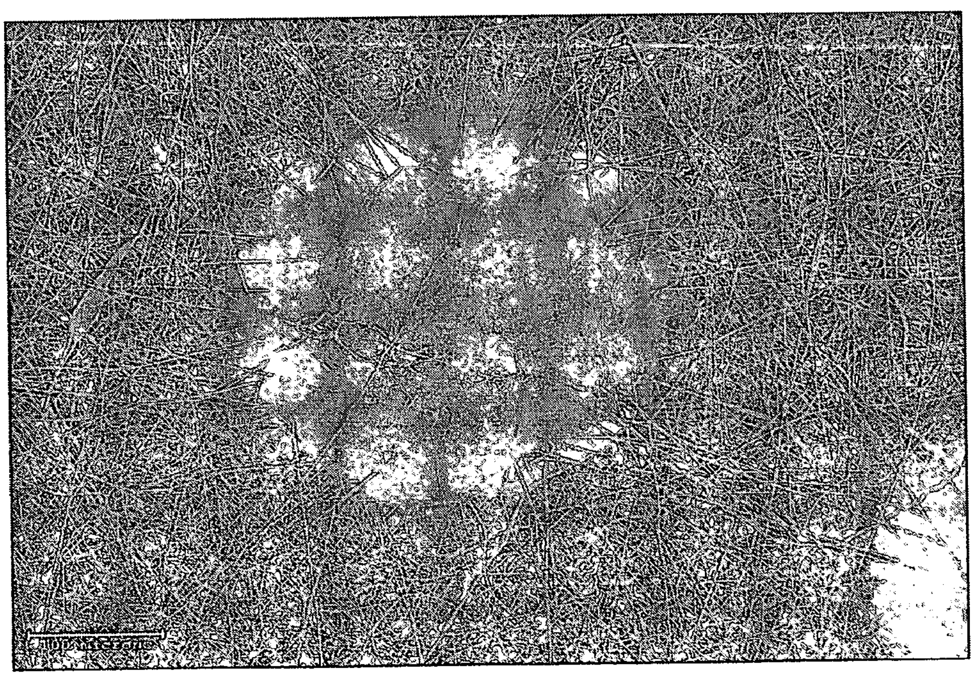


Fig. 10



100 microns

APPLICATION DATA SHEET

Electronic Version v14
Stylesheet Version v14.0

Title of Invention	EMULSION-BASED CONTROL OF ELECTROSPUN FIBER MORPHOLOGY

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